Vaccines + Biologics:

Clinical Considerations and Evidence-Based Recommendations

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Learning Objectives

- Identify clinical concerns about vaccines in patients receiving biologics
- Examine available data on concomitant use of vaccines and biologics
- Recommend evidence-based vaccination options to patients on biologics

Current Situation: Allergists/Immunologists

- Biologics for atopic disease
  - Dupilumab
- Increasing use, indications
- Vaccination challenges

Immunologic Concerns -> Clinical Concerns

Impaired vaccine immunogenicity

Risk of vaccine-strain infection with live vaccines

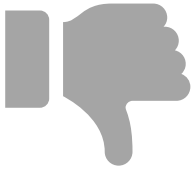
Altered cytokine balance

Durability of immune response

Safety concerns re: underlying disease

Nat Rev Drug Discov. 2016;15(1):35-50.
Clin Infect Dis. 2014;58(3):309-318.
Adv Immunol. 2009;101:191-236.
Cytokine. 2015;75(1):25-37.
Science. 2003;300(5625):1527-1528.
Clin Immunol. 2022;244:109130.
J Eur Acad Dermatol Venereol. 2018;32(5):657-682.

Regulatory Perspectives



Package Insert:

"Avoid use of live vaccines“

Basis for warning:

Lack of data

Challenges in

clinical practice

Dupixent Package Insert. Accessed April 27, 2025. www.regeneron.com/downloads/dupixent_fpi.pdf

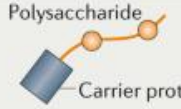
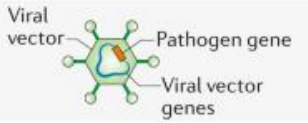
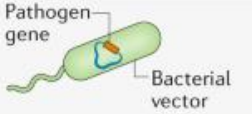
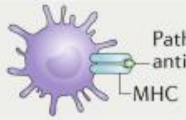
Types of Vaccines

Non-Live Vaccines:

- Inactivated pathogens, subunits, toxoids, nucleic acids
- Generally considered safe but questions about efficacy

Live Attenuated Vaccines:

- Weakened but replicating pathogens
- Theoretical risk of vaccine-strain infection

Type of vaccine		Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)		Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism		Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid		Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle		Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate		*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored		Ebola	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored		Experimental	–
Antigen-presenting cell		Experimental	–

Nat Rev Immunol. 2021; 21:83–100.

Practical Clinical Dilemmas

Pediatric patients requiring routine live vaccines

Travel requirements (e.g., yellow fever)

Outbreak management

Timing considerations

Risk-benefit assessment without robust evidence

Am J Clin Dermatol. 2021;22(4):443-455.
J Cutan Med Surg. 2019;23(1):50-74.
Am Acad Dermatol. 2020;83(5):1282-1293.
J Allergy Clin Immunol Glob. 2022;1(1):9-15.
CDC. Recommended Adult Immunization Schedule for ages 19+, United States, 2024.

Non-Live Vaccines: TDaP, MPSV4

- Blauvelt et al. (2019) RCT
  - 178 adults with AD on dupilumab
  - Comparable immune responses between dupilumab and placebo
  - No effect on T-cell dependent or independent responses

J Am Acad Dermatol. 2019;80(1):158-167.e1.

Non-Live Vaccines: COVID-19 mRNA

- Runnstrom et al. (2024) prospective, observational study
  - Lower SARS-CoV-2 antibody levels in patients on biologics
  - Reduced neutralization ability
  - Lower frequencies of virus-specific B and T cells
- Abadeh and Lee case report (2023)
  - Failed response while on dupilumab
  - Successful response after holding therapy

J Allergy Clin Immunol. 2024;154(2):435-446.
J Allergy Clin Immunol Glob. 2023;2(1):118-119.

Non-Live Vaccines: COVID-19 mRNA

- Ungar et al. (2022) retrospective study
  - 180 patients age 12+ with AD; 101 treated with dupilumab
  - No differences in SARS-CoV-2 IgG levels in dupilumab group 14 days after 2nd vaccine
- Ungar et al. (2023)
  - Dupilumab patients w/ higher IFN-gamma-producing cells; suggests enhanced T-cell immunity
- Wieske et al. (2022) – observational study: Dutch patients with immune disorders
  - 58 on dupilumab
  - 98% seroconversion after COVID-19 vaccination*; comparable to controls
  - Diminished boosting effect (0.64 fold-change vs controls) in dupilumab group between 2nd, 3rd doses

Ann Allergy Asthma Immunol. 2022;128(6):734-736.
Allergy. 2023;78(2):571-574.
Lancet Rheumatol. 2022;4(5).

Non-Live Vaccines: Clinical Implications

- General safety established
- Potentially reduced, but clinically adequate
- No evidence that treatment interruption is necessary
- Recommended seasonal vaccinations should continue

Live Vaccines: Yellow Fever

- Wechsler et al. (2022) - LIBERTY ASTHMA TRAVERSE
  - 37 patients who received yellow fever vaccine after stopping dupilumab
  - All achieved seroprotection despite therapeutic dupilumab levels
  - No instances of disseminated infection
  - Only one non-serious adverse event reported

J Allergy Clin Immunol Glob. 2022;1(1):9-15.

Live Vaccines: MMR, Varicella

- Siegfried et al. (2024) case series
  - 9 children with severe AD receiving MMR/varicella vaccines
  - 5 with ≤12 weeks between dupilumab and vaccination
  - No adverse events reported

Pediatr Dermatol. 2024;41(2):204-209.

Live Vaccines: MMR, Varicella (*New Evidence)

- Hughes et al. (2025) retrospective review
  - 313 pediatric patients on dupilumab or methotrexate
  - 5 received MMRV while on dupilumab
  - No adverse events for up to 6 months after immunization
  - Challenges theoretical basis for blanket prohibition

Pediatr Dermatol. 2025;42(2):284-288.

A systematic review and expert Delphi Consensus recommendation on the use of vaccines in patients receiving dupilumab: A position paper of the American College of Allergy, Asthma and Immunology

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Ann Allergy Asthma Immunol. 2024;133(2):286-294.

2024 Delphi Consensus: Non-Live Vaccines

- Dupilumab does not appear to affect protective antibody titers
- Treatment interruption not necessary for administration
- Seasonal influenza vaccination should continue
- No evidence that immunization causes exacerbation

Ann Allergy Asthma Immunol. 2024;133(2):286-294.

2024 Delphi Consensus: Live Vaccines

- No evidence that co-administration with dupilumab is unsafe
- Absence of studies is multifactorial
- Case-by-case consideration weighing risks of action versus inaction
- If possible, give 4+ weeks before starting dupilumab
- Antibody level measurement may be an option

Ann Allergy Asthma Immunol. 2024;133(2):286-294.

General Recommendations

- Pre-treatment assessment and vaccination when possible
- Shared decision-making approach
- Document discussions about risks/benefits
- Consider individual circumstances: age, exposure risk, disease severity

Ann Allergy Asthma Immunol. 2024;133(2):286-294.
Am J Clin Dermatol. 2021;22(4):443-455.
BMJ Open. 2020;10(3).
MMWR Recomm Rep. 2011;60(2):1-64.

Recommendations: Non-Live Vaccines

- Continue according to recommended schedules
- No need to interrupt biologic therapy
- Consider antibody monitoring for high-risk patients
- Additional doses may be appropriate for suboptimal responses

J Allergy Clin Immunol. 2024;154(2):435-446.
Allergy. 2023;78(2):571-574.
Am J Clin Dermatol. 2021;22(4):443-455.
Pediatrics. 2023;152(4).
Vaccine. 2016;34(27):3141-3148.

Recommendations: Live Vaccines

- When possible, administer at least 4 weeks before starting biologic
- For patients already on therapy:
  - Case-by-case assessment
  - Consider disease risk vs. theoretical vaccine risks
  - Evaluate emerging safety evidence
  - Specialist consultation when appropriate

J Allergy Clin Immunol Glob. 2022;1(1):9-15.
Am J Clin Dermatol. 2021;22(4):443-455.
Ann Rheum Dis. 2011;70(10):1704-1712.
CDC/ACIP Guidelines: Altered immunocompetence.

Special Considerations: MMR and Varicella

- Growing evidence suggests these may be safer than previously thought
- Weigh risk of natural infection versus risk of vaccine
- Consider incidence, prevalence rates
- Close monitoring for adverse events

Pediatr Dermatol. 2024;41(2):204-209.
Pediatr Dermatol. 2025;42(2):284-288
Rheumatology (Oxford). 2009;48(2):144-148..

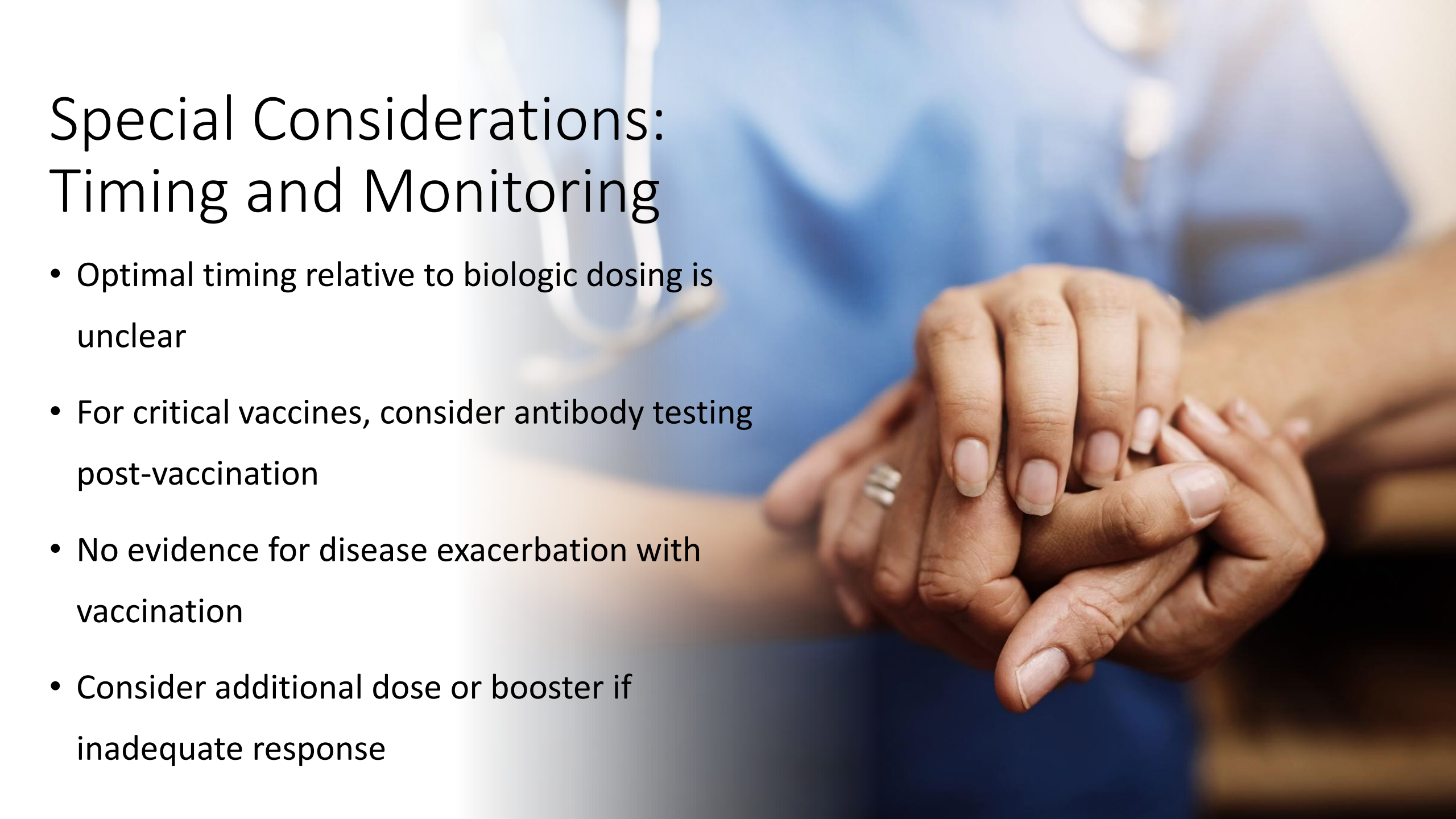
Special Considerations: Yellow Fever

- Travel requirements often cannot be waived
- Consider temporary discontinuation of biologic
- Wechsler study suggests good immunogenicity, safety
- Risk assessment based on destination is essential

J Allergy Clin Immunol Glob. 2022;1(1):9-15.

Special Considerations: Timing and Monitoring

- Optimal timing relative to biologic dosing is unclear
- For critical vaccines, consider antibody testing post-vaccination
- No evidence for disease exacerbation with vaccination
- Consider additional dose or booster if inadequate response



Research Gaps

- Larger, prospective studies
- Pediatric data, especially for primary immunization
- Durability of protection
- Optimization strategies
- Novel biologics

Case Scenarios

- Pediatric patient with EoE needing MMR before school entry
- Adult with chronic urticaria planning travel requiring yellow fever vaccination
- Adolescent with severe eczema who needs varicella vaccine
- Adult on asthma biologic during *the next* pandemic

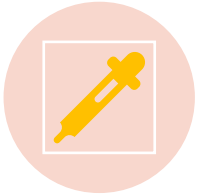
Practical Algorithm

- Is the patient on biologic therapy?
- Is the vaccine live or non-live?
- What is the risk/likelihood of natural infection?
- Is temporary interruption feasible?
- Is antibody monitoring available?

Key Takeaways

Non-live vaccines are safe during biologic therapy

Emerging data on live vaccines may change approach



Pre-treatment vaccination ideal when possible

Risk/benefit assessment for patients on therapy

Shared decision-making essential